The Royal College of Surgeons of England

ORTHOPAEDICS

Ann R Coll Surg Engl 2008; **90**: 332–335
doi 10.1308/003588408X285946

Gastric protection and gastrointestinal bleeding with aspirin thromboprophylaxis in hip and knee joint replacements

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ABSTRACT

INTRODUCTION Upper gastrointestinal (GI) bleeding in patients who undergo hip and knee arthroplasty tends to be associated with non-steroidal anti-inflammatory drug use, steroid intake, pre-existing peptic ulcers and smoking. The use of aspirin for thromboprophylaxis is an added risk for the occurrence of GI bleed. The aim of this study was to determine the incidence of upper GI bleeding and whether the use of peri-operative oral ranitidine reduces the incidence of upper GI bleeding when aspirin thromboprophylaxis is used for hip and knee arthroplasty.

PATIENTS AND METHODS Data from 1491 and 886 patients who underwent hip and knee replacements at the James Cook University Hospital (group 1) and at Friarage Hospital, Northallerton (group 2), respectively, were analysed in retrospect. All patients received 150 mg of aspirin per day for a period of 6 weeks from the day of surgery. Additionally, patients operated at the Friarage Hospital received 300 mg of oral ranitidine per day, for three postoperative days.

RESULTS We observed that patients in group 1 had a higher incidence of overt upper GI haemorrhage, which was statistically significant (P <0.014) compared to patients in group 2.

CONCLUSIONS Based on this experience, we recommend the use of peri-operative gastric protection with ranitidine when aspirin is used for thromboprophylaxis in hip and knee arthroplasty.

KEYWORDS

Aspirin – Gastrointestinal bleeding – Histamine blockers

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Deep vein thrombosis (DVT) and pulmonary embolism are recognised complications of hip and knee replacement arthroplasty. Some form of thromboprophylaxis is, therefore, commonly used for patients undergoing hip and knee arthroplasty. The Scottish Intercollegiate Guidelines Network[1] recommends the use of aspirin for thromboprophylaxis in patients undergoing total hip and knee arthroplasty.

Aspirin, in low doses, blocks thromboxane A2 synthesis,[2] which is a potent vasoconstrictor and promotes platelet aggregation. Higher doses of aspirin are ineffective and inhibit prostacyclin synthesis, which is a natural antithrombotic, produced by the vascular endothelium.[2,3] It has limited efficacy in reducing DVT and pulmonary embolism but is easy to administer and requires no monitoring. It carries the risk of GI bleeding, when concomitantly used with other non-steroidal anti-inflammatory drugs (NSAIDs), steroids and in proven gastric and duodenal ulcers.[3]

The side effects of aspirin are mainly gastrointestinal which can be acute or chronic.[4,5] Short-term aspirin produces gastric ulcers, anaemia, and gastrointestinal haemorrhage. Prostaglandin synthesis inhibition has been proposed as a potential mechanism for gastrointestinal bleeding. Aspirin by inhibiting thromboxane A2 synthesis reduces platelet aggregation and vasoconstriction. The action of aspirin on platelet cyclooxygenase is permanent, increasing the life of the platelets (7–10 days). Repeated doses of aspirin produces a cumulative effect on platelet function in addition to its gastric mucosal irritation. The combined ulcerogenic and antithrombotic effects predispose bleeding tendencies commonly seen with aspirin. Randomised control studies on aspirin-related gastrointestinal bleeds suggest that the risk of peptic ulcer disease was 1.3 and of upper GI symptoms 1.7. Fatal bleeds are rare and toxicity is dose-related.[6]

Aspirin-induced gastric injury assessed by bleeding and changes at endoscopy are greatest in the first week and there is evidence that adaptation occurs after a period of 2–8 weeks of continuous ingestion.[7–9] Erythema of gastric mucosa, erosions and ulcerations are commonly seen in patients with rheumatic diseases on aspirin. Bleeding usually originates in the stomach and proximal duodenum and is due to the local effects of aspirin induced by oral administration.[10] Histamine blockers reduce the gastric side effects of aspirin.[11]

We present our experience with aspirin thromboprophylaxis the risk of gastrointestinal bleeding with aspirin and suggest measures to reduce this risk.

Patients and Methods

All 2377 patients who underwent hip and knee replacements between 2002 and 2005 were included in the study. Of these, 1491 patients were admitted and operated at the James Cook University Hospital, Middlesbrough (group 1) and 886 patients were admitted and operated at the Friarage Hospital, Northallerton (group 2). Patients with the above operations and those with symptomatic gastrointestinal bleeds were identified from the hospital computer database using the universal coding system. We recognise the limitation of the coding system in that it does not indicate the severity of the bleed and its clinical implications. There was no documented evidence of symptomatic gastrointestinal bleeding in either group prior to the contemplated orthopaedic procedure. There were no exclusions from the study.

This is a retrospective study and, from the available data, the co-morbidities in both the groups were comparable. However, subtle differences exist regarding patient populations being compared in terms of the economic and social strata and demographic profiles.

All patients had pre-operative assessments in order to determine co-morbidity and fitness for surgery. Thromboprophylaxis was initiated with 150 mg of aspirin from the day of surgery postoperatively and for a period of 6 weeks thereafter. Patients in group 2 additionally received oral ranitidine 300 mg/day starting the day before surgery, and continued for 3 days postoperatively. Antibiotic prophylaxis with three doses of a second generation cephalosporin (cefuroxime 750 mg) postoperatively was given in addition to a loading dose of 1500 mg at induction. Patients were operated either under regional or general anaesthesia, as deemed appropriate by the anaesthetist.

All patients were mobilised within 48 h postoperatively under the direction of a trained physiotherapist. Patients were discharged on successful recovery from surgery and followed up in the joint replacement clinic.

The notes of patients who had documented gastrointestinal bleeding in the form of haemetamesis and/or melena following surgery were retrieved and analysed from the computer database. These were the patients who had upper GI bleeding while in the hospital following the operation or referred to the upper GI department after discharge from orthopaedic care following the operation. Patients with late bleeds were referred the upper GI care by general practitioners and other surgical departments. Case notes were retrieved in these patients. Details regarding the orthopaedic surgical procedure, gastrointestinal bleed, associated diseases and medications, and in-hospital mortality with reference to gastric bleed were recorded and studied for any correlations. The results were analysed statistically using the chi-square test to compare the results for significance and deriving a *P*-value, using SPSS v12, (SPSS Inc., IL, USA)

Results

Fifteen patients (8 females and 7 males) with an average age of 76 years (14 in group 1 and 1 in group 2) had symptomatic gastrointestinal bleeding. Eight patients had undergone total hip replacements which included five primary and three revision procedures. The indications for total hip replacement in patients with gastrointestinal bleeding were primary degenerative osteoarthritis in five patients, traumatic hip fracture in two patients and avascular necrosis of the hip with secondary osteoarthritis related to chronic alcoholism in one patient. Two patients with severe osteoarthritis of the hip were under the cover of steroids for associated Crohn's disease and chronic obstructive pulmonary disease, respectively. These patients had associated problems of fistulae and infection necessitating multiple procedures in the form of wound wash-outs, debridements and girdlestone arthroplasty for the hip problem.

Seven patients underwent total knee replacement, which included four primary procedures and three revisions for primary degenerative osteoarthritis of the knee. Eight patients had haemetamesis and seven had melena requiring resuscitation with intravenous fluids in all patients, blood transfusions in two patients and, subsequently, bleeding control measures by a gastroenterologist. Of these, seven patients bled on the day of surgery, one patient after 48 h, three patients between 3–7 months and four patients around 1 year after surgery. Peri-operative gastrointestinal bleeding (less than 48 h) manifested clinically as haemetamesis and as melena in patients who had GI bleed 3 months after surgery. One patient who had peri-operative ranitidine prophylaxis had symptomatic peri-operative gastrointestinal bleeding. There was no relationship between the orthopaedic procedure performed and the occurrence of bleeding.

All patients with GI bleeds had endoscopy. Two patients had normal findings on endoscopy. Duodenal ulcers were

found in six patients, haemorrhagic gastritis in three patients, benign gastric ulcers in two patients, one patient had normal gastric and duodenal mucosa but a Mallory Weiss tear. One patient with Crohn's disease had extensive mucosal changes consistent with the disease on endoscopy and a bleeding gastric ulcer.

There were no in-patient deaths in this group of patients. At the point when this review was being done, four patients had died a year following the replacement, three due to medical problems and one due to a perforated duodenal ulcer. The exact cause of death could not be confirmed by autopsy.

Statistically, patients in group 1 had a higher incidence of GI bleeding which was significant ($P < 0.014$) and continued to be significant at $P < 0.05$ even when the late bleeds at 1 year were removed from the data.

From the pooled data of both groups, there were 18 reported patients with symptomatic pulmonary embolism (0.75%), three of which were fatal (0.12%), phlebitis of deep leg veins and femoral veins in 31 patients (1.3%), deep vein thrombosis in 34 patients (1.43%), five of whom had embolic episodes, postoperative infection in 22 patients (1.13%), and postoperative haemorrhage in five patients (0.2%). Thrombo-embolic phenomena and pulmonary embolism were confirmed by autopsy in the three suspected cases.

Discussion

Although there is agreement that the aim of any thromboprophylaxis in total joint replacements is to prevent deep venous thrombosis and pulmonary embolism, a clear consensus on the choice of regimen does not exist.[12,13] It has been our policy to follow the SIGN guidelines[1] and recommendations of the Pulmonary Embolism Prevention trial, and be guided by clinical end-points to document the benefits and risks of aspirin therapy.

The Pulmonary Embolism Prevention trial clearly indicates the occurrence of increased bleeding tendencies with aspirin.[14,15] Higher doses of aspirin are ineffective and inhibit prostacyclin synthesis, which is a natural antithrombotic produced by the vascular endothelium.[2,3]

The age of the patient, stress of surgery, pre-operative fasting, associated medical diseases and their medications increase the risk of gastrointestinal bleeding. The safety margin profile of aspirin, as mentioned in the literature, becomes blurred in these situations. The majority of the bleeds that occurred in our study fall into the early group which possibly is due to the direct toxicity of aspirin on the gastric mucosa. Adaptation which normally occurs in the later weeks of therapy will probably explain the smaller number of late bleeds. The risk is particularly increased in the elderly population where a careful enquiry is needed. Ingestion of non-steroidal inflammatory agents is common particularly in elderly people but patients may fail to declare such information unless specific enquiry is made.[16] Most patients in our study were on medication for concurrent medical illnesses and we could not totally rule out the possibility of them being on commercially available non-steroidal anti-inflammatory drugs from the available data. Erosive oesophagitis is common in patients with upper gastrointestinal bleeding taking low-dose aspirin.[17]

We have considered only symptomatic patients in our study and the supposedly normal patient population on aspirin prophylaxis may be having sub-clinical GI bleeds which could clinically manifest at varied intervals with the continued use of aspirin. It is not clear as to how long the effects of aspirin will persist after the cessation of therapy; for this reason, we cannot explain gastrointestinal bleeds that occurred at various periods following replacements as being solely due to aspirin.

Although this is a retrospective study, we believe our observations are significant in that these patients are likely to represent the 'tip of the iceberg' of a larger population at risk of GI bleeds. Our findings indicate that H2 blockers have a definite role in the prevention of symptomatic gastrointestinal haemorrhages in this cohort of patients.

Conclusions

When aspirin thromboprophylaxis is used in hip and knee replacements, there is a small associated risk (0.63%) of overt symptomatic gastrointestinal bleeding that requires investigation and treatment. Our observations indicate that a short period of gastric protection with peri-operative ranitidine for 3 days can reduce the risks of GI bleeds.

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